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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/067,638	04/28/1998	LEX M. COWSERT	ISIS-2960	1414

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EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/067,638

Applicant(s)

COWSERT ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/3/05.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 83-87 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 83-87 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 83-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Applicant's arguments filed 11/3/05 have been fully considered but they are not persuasive. Applicant is thanked for repeating arguments with regard to support for the limitations of the claims. Unfortunately, the portions of the specification indicated by applicant do not provide support for the limitations added in the amendment filed 2/14/05 for the reasons previously set forth. The reasons are reiterated below for further clarity.

A system for preparing a set of oligonucleotides wherein a computer system FIRST prepares a virtual library of oligonucleotide sequences, then reduces the number of sequences, is new matter. The originally filed claims were directed to methods comprising in silico evaluation of a library of oligonucleotides according to defined criteria (e.g. claim 7) or comprising generating a library of nucleobase compounds in silico according to defined criteria (e.g. claim 8). It is noted that claim 7 and similar original claims did not recite first generating a library of oligonucleotides for evaluation. As many databases of oligonucleotide sequences are known in the art (see the NCBI compendium), the library could have been supplied or selected from a database; generation of a virtual library is not inherent. The originally filed specification on page 8 teaches that in a method and system for generating compounds with desired

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properties, a target nucleic acid sequence is provided or selected, and a library of nucleobase sequences is generated *in silico according to defined criteria*. Original Figure 1 also discloses generating a list of oligonucleotide sequences *with desired properties* BEFORE a step of synthesizing those with desired activities. Original Figure 4 discloses generating oligonucleotide sequences capable of hybridizing to a target sequence. In all cases, the list or virtual library generated is one comprising sequences with selected properties; i.e. one which is already “reduced”. Nowhere do the originally filed claims or specification teach preparing or generating a virtual library before any step of selection or reduction.

IN response to applicant’s arguments for support in the instant specification, page 19 of the specification discloses a step of generating a series of oligonucleotide sequences *of desired length and capable of hybridizing to a target*; i.e. the sequences in the generated library are not random, but are generated according to defined criteria. Thus, contrary to applicant’s argument, page 19 does not provide support for the broader limitation of the claims. Pages 22-23 are directed to calculation of thermodynamic properties, and do not disclose generating a library. Pages 24-26 disclose targeting to oligonucleotides to functional regions; which supports the “reduction” step of the instant claims, but not the “generating of a library” prior to the reduction step. Page 65 discloses generation of nucleotides of a particular length and hybridization properties (those with selected properties), but does not disclose computer generation of a random library of oligonucleotides. Pages 103-105 do not disclose anything with regard to generation of a library. Figure 4 discloses, in steps (302) and (304) selecting a length and generating all possible oligonucleotide sequences capable of hybridizing to a target sequence; again, this is support for generating a library according to defined criteria, but is not support for generating a random library, as encompassed by the claims. The other figures argued by applicant do not disclose generating a library of oligonucleotide sequences prior to a selection

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or reduction step. For these reasons, applicant's arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 83 and 85-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over AGRAFIOTIS et al. (US 5,463,564) in view of HYNDMAN et al. (Biotechniques 20(6): 1090 (1996)) and NICKERSON et al. (PNAS 87 : 8923 (1990)) and further in view of GRAYBILL et al. (US 6,127,191, filed 12/3/1996).

Claims 83-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over AGRAFIOTIS et al. (US 5,463,564) in view of HYNDMAN et al. (Biotechniques 20(6): 1090 (1996)), NICKERSON et al. (PNAS 87 : 8923 (1990)), and either ALBERTSEN et al. (US 5,352,775) or CUTTING et al. (US 5,407,796), and further in view of GRAYBILL et al. (US 6,127,191, filed 12/3/1996).

Applicant presents arguments encompassing all the rejections, therefore the response will address the arguments in toto. Applicant's arguments filed 11/3/05 have been fully considered but they are not persuasive. Applicant argues that the references do not teach creating a library of oligonucleotides, reducing the library using the criteria of the instant claims, then generating only those compounds that remain following the reduction step. Applicant further argues that AGRAFIOTIS teaches a library with increasing diversity, not one which is reduced according to defined criteria.

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In response, applicant is reminded that the rejection is made over a combination of references wherein AGRAFIOTIS teaches generation of a virtual library of compounds prior to an actual synthesis step and specifically teaches that such libraries may comprise oligonucleotides (col. 1, lines 32-43) and teaches that the point of making such libraries is to screen them for desirable properties (col's 1-2). In the combination of references previously set and reiterated above, GRAYBILL teaches an iterative process of selecting compounds with desired properties wherein a virtual library of compounds is generated, then evaluated for specific physical and biological properties (col. 14, lines 40-61), while HYNDMAN teaches screening for the particular properties recited in the instant claims (see e.g. the HYB simulator of HYNDMAN for selecting probes, p. 1091). Thus, the examiner maintains that the combination of references does make obvious generating a library of oligonucleotides (AGRAFIOTIS), reducing the library by a process of selection based on targeting a functional region of a selected nucleic acid (HYNDMAN and GRAYBILL), and synthesizing only those oligonucleotides resulting from the reduction step (GRAYBILL). The examiner also maintains that the other limitations of the claims (not argued by applicant) are also taught/made obvious by the combination of references for the reasons and motivations previously set forth. For these reasons and those previously set forth, the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 83 and 85-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 55, 56, 58-72, 74-87, and 99-102 of copending Application No. 09/295,463. Although the conflicting claims are not identical, they are not patentably distinct from each other for reasons previously of record. As the claims have not been amended to be patentably distinct and applicant has not presented any arguments with regard to this rejection, the rejection is maintained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In the response filed 11/3/05, applicant "agrees" to filed a terminal disclaimer upon indication of allowable subject matter. Applicant is reminded that double patenting rejections may not be held in abeyance, therefore until such time as a terminal disclaimer is filed, or until the claims of the instant application and/or the '463 application are amended to overcome the rejection, the rejection will be maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
1/23/06